

- - 1. (Thrice amended) A composition comprising nucleic acid molecules [containing a human sequence encoding insulin-like growth factor (hIGF)] comprising a nucleic acid sequence substantially free of nucleic acid molecules not [containing] comprising said [hIGF] nucleic acid sequence, wherein said [hIGF] nucleic acid sequence is selected from the group consisting of:

(a) 5'-GGA CCG GAG ACG CUC UGC GGG GCU GAG CUG GUG GAU GCU CUU CAG UUC GUG UGU GGA GAC AGG GGC UUU UAU UUC AAC AAG CCC ACA GGG UAU GGC UCC AGC AGU CGG AGG GCG CCU CAG ACA GGU AUC GUG GAU GAG UGC UGC UUC CGG AGC UGU GAU CUA AGG AGG CUG GAG AUG UAU UGC GCA CCC CUC AAG CCU GCC AAG UCA GCU-3', wherein U can also be T;

(b) 5'-GCU UAC CGC CCC AGU GAG ACC CUG UGC GGC GGG GAG CUG GUG GAC ACC CUC CAG UUC GUC UGU GGG GAC CGC GGC UUC UAC UUC AGC AGG CCC GCA AGC CGU GUG AGC CGU CGC AGC CGU GGC AUC GUU GAG GAG UGC UGU UUC CGC AGC UGU GAC CUG GCC CUC CUG GAG ACG UAC UGU GCU ACC CCC GCC AAG UCC GAG-3', wherein U can also be T;

(c) a nucleic acid sequence[s] complementary to (a) or (b); [and]

(d) a fragment[s] of [(a), (b) or (c)] (a) or (b) that [are] is at least 18 bases in length [and which will selectively hybridize to human genomic DNA encoding hIGF]; and

(e) a fragment of (c) that is at least 18 bases in length.

2. (Thrice amended) A composition according to claim 1 wherein said [hIGF is

hIGF-I and said hIGF] nucleic acid sequence is sequence (a).

3. (Thrice amended) A composition according to claim 1 wherein said [hIGF is

hIGF-I and said hIGF] nucleic acid sequence is sequence (b).

6. (Thrice amended) A composition according to claim 1 wherein said nucleic acid

molecules are DNA, and U is T.

7. (Thrice amended) A composition according to claim 1 wherein said nucleic acid

molecules are RNA, and U is U.

8. (Thrice amended) A composition comprising cellular hosts transformed by a

heterologous DNA sequence substantially free of cellular hosts that do not contain said heterologous

DNA sequence, wherein said heterologous DNA sequence is a human sequence encoding insulin-

like growth factor (hIGF)] comprises a nucleic acid sequence selected from the group consisting of:

(a) 5'-GGA CCG GAG ACG CTC TGC GGG GCT GAG CTG GTG GAT GCT CTT

CAG TTC GTG TGT GGA GAC AGG GGC TTT TAT TTC AAC AAG CCC ACA GGG TAT

GGC TCC AGC AGT CGG AGG GCG CCT CAG ACA GGT ATC GTG GAT GAG TGC TGC

TTC CGG AGC TGT GAT CTA AGG AGG CTG GAG ATG TAT TGC GCA CCC CTC AAG

CCT GCC AAG TCA GCT-3';

(b) 5'-GCT TAC CGC CCC AGT GAG ACC CTG TGC GGC GGG GAG CTG

*Def 51* GTG GAC ACC CTC CAG TTC GTC TGT GGG GAC CGC GGC TTC TAC TTC AGC AGG  
CCC GCA AGC CGT GTG AGC CGT CGC AGC CGT GGC ATC GTT GAG GAG TGC TGT  
TTC CGC AGC TGT GAC CTG GCC CTC CTG GAG ACG TAC TGT GCT ACC CCC GCC  
AAG TCC GAG-3';

(c) a nucleic acid sequence[s] complementary to (a) or (b); [and]

(d) a fragment[s] of [(a), (b) or (c)] (a) or (b) that [are] is at least 18 bases in length  
[and which will selectively hybridize to human genomic DNA encoding hIGF]; and

(e) a fragment of (c) that is at least 18 bases in length.

9. (Thrice amended) A composition according to claim 8 wherein said [heterologous DNA] nucleic acid sequence is selected from the group consisting of sequences (a), (b) and (c).

*D2 cont* 10. (Thrice amended) A composition according to claim 9 wherein said [hIGF is hIGF-I and said heterologous DNA] nucleic acid sequence is sequence (a).

*Def 72* 11. (Thrice amended) A composition according to claim 9 wherein said [hIGF is hIGF-II and said heterologous DNA] nucleic acid sequence is sequence (b).

*B* 12. (Twice Amended) A composition according to claim 10 wherein said [heterologous DNA] nucleic acid sequence comprises the following sequence:

5'-CTG GCG CTG TGC CTG CTC ACC TTC ACC AGC TCT GCC ACG GCT GGA CCG GAG

ACG CTC TGC GGG GCT GAG CTG GTG GAT GCT CTT CAG TTC GTG TGT GGA GAC  
AGG GGC TTT TAT TTC AAC AAG CCC ACA GGG TAT GGC TCC AGC AGT CGG AGG  
GCG CCT CAG ACA GGT ATC GTG GAT GAG TGC TGC TTC CGG AGC TGT GAT CTA  
AGG AGG CTG GAG ATG TAT TGC GCA CCC CTC AAG CCT GCC AAG TCA GCT CGC  
TCT GTC CGT GCC CAG CGC CAC ACC GAC ATG CCC AAG ACC CAG AAG GAA GTA  
CAT TTG AAG AAC GCA AGT AGA GGG AGT GCA GGA AAC AAG AAC TAC AGG ATG-  
3'.

13. (Twice Amended) A composition according to claim 11 wherein said  
[heterologous DNA] nucleic acid sequence comprises the following sequence:

5'-ATG GGA ATC CCA ATG GGG AAG TCG ATG CTG GTG CTT CTC ACC TTC TTG GCC  
TTC GCC TCG TGC TGC ATT GCT GCT TAC CGC CCC AGT GAG ACC CTG TGC GGC  
GGG GAG CTG GTG GAC ACC CTC CAG TTC GTC TGT GGG GAC CGC GGC TTC TAC  
TTC AGC AGG CCC GCA AGC CGT GTG AGC CGT CGC AGC CGT GGC ATC GTT GAG  
GAG TGC TGT TTC CGC AGC TGT GAC CTG GCC CTC CTG GAG ACG TAC TGT GCT  
ACC CCC GCC AAG TCC GAG AGG GAC GTG TCG ACC CCT CCG ACC GTG CTT CCG  
GAC AAC TTC CCC AGA TAC CCC GTG GGC AAG TTC TTC CAA TAT GAC ACC TGG  
'AAG CAG TCC ACC CAG CGC CTG CGC AGG GGC CTG CCT GCC CTC CTG CGT GCC  
CGC CGG GGT CAC GTG CTC GCC AAG GAG CTC GAG GCG TTC AGG GAG GCC AAA  
CGT CAC CGT CCC CTG ATT GCT CTA CCC ACC CAA GAC CCC GCC CAC GGG GGC  
GCC CCC CCA GAG ATG GCC AGC AAT CGG AAG TGA-3'.

D3  
cont

14. (Twice Amended) A composition according to claim 9 wherein said [heterologous DNA] nucleic acid sequence is located on a plasmid that replicates in said cellular host.

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18. (Thrice amended) A composition consisting essentially of nucleic acid molecules [containing a human sequence encoding insulin-like growth factor (hIGF)] comprising a nucleic acid sequence selected from the group consisting of:

(a) 5'-GGA CCG GAG ACG CUC UGC GGG GCU GAG CUG GUG GAU GCU CUU CAG UUC GUG UGU GGA GAC AGG GGC UUU UAU UUC AAC AAG CCC ACA GGG UAU GGC UCC AGC AGU CGG AGG GCG CCU CAG ACA GGU AUC GUG GAU GAG UGC UGC UUC CGG AGC UGU GAU CUA AGG AGG CUG GAG AUG UAU UGC GCA CCC CUC AAG CCU GCC AAG UCA GCU-3', wherein U can also be T;

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(b) 5'-GCU UAC CGC CCC AGU GAG ACC CUG UGC GGC GGG GAG CUG GUG GAC ACC CUC CAG UUC GUC UGU GGG GAC CGC GGC UUC UAC UUC AGC AGG CCC GCA AGC CGU GUG AGC CGU CGC AGC CGU GGC AUC GUU GAG GAG UGC UGU UUC CGC AGC UGU GAC CUG GCC CUC CUG GAG ACG UAC UGU GCU ACC CCC GCC AAG UCC GAG-3', wherein U can also be T;

(c) a nucleic acid sequence[s] complementary to (a) or (b); [and]

(d) a fragment[s] of [(a), (b) or (c)] (a) or (b) that [are] is at least 18 bases in length [and which will selectively hybridize to human genomic DNA encoding hIGF]; and

(e) a fragment of (c) that is at least 18 bases in length.

19. (Twice Amended) A composition according to claim [9] 8 wherein said cellular host is *E. coli* strain HB101(phigf1).

20. (Twice Amended) A composition according to claim 1 wherein said nucleic acid molecules are plasmid phigf1 molecules.

21. (Twice Amended) A composition according to claim [9] 8 wherein said cellular host is *E. coli* strain HB101(phigf2).

22. (Twice Amended) A composition according to claim 1 wherein said nucleic acid molecules are plasmid phigf2 molecules. -

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Please amend added claims 23-48 as follows.

Please cancel previously submitted claims 23-41 and 44-48 and replace with thrice amended claims 23-28 and 31-35, twice amended claims 29-30 and 40-43, and once amended claims 36-39 and 44-48 as follows.

23. A method of producing a polypeptide comprising an amino acid sequence of Fig. 1 or Fig. 2 in a suitable host cell transformed with a polynucleotide encoding said polypeptide, wherein said polynucleotide comprises a nucleic acid sequence encoding said amino acid sequence

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selected from the group consisting of the nucleic acid sequences of claims 2 and 3.

24. A method of producing a polypeptide comprising an amino acid sequence of Fig. 1 or Fig. 2, comprising introducing into a suitable host cell a nucleic acid molecule comprising a polynucleotide encoding said polypeptide, wherein said polynucleotide comprises a nucleic acid sequence encoding said amino acid sequence selected from the group consisting of the nucleic acid sequences of claims 2 and 3.

25. The method of claim 23 wherein said amino acid sequence is IGF-I and said nucleic acid sequence is sequence (b).

26. The method of claim 23 wherein said amino acid sequence is IGF-II and said nucleic acid sequence is sequence (b).

27. A method of producing a polypeptide comprising the amino acid sequence of Fig. 1 in a suitable host cell transformed with a polynucleotide encoding said polypeptide, wherein said polynucleotide comprises the nucleic acid sequence of claim 4, which method comprises expressing said polynucleotide in said host cell.

28. A method of producing a polypeptide comprising the amino acid sequence of Fig. 2 in a suitable host cell transformed with a polynucleotide encoding said polypeptide, wherein

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said polynucleotide comprises the nucleic acid sequence of claim 5, which method comprises  
expressing said polynucleotide in said host cell.

29. The method of claim 24 wherein said nucleic acid molecule is the plasmid  
phigf1.

30. The method of claim 24 wherein said nucleic acid molecule is the plasmid  
phigf2.

31. A method of producing a polypeptide comprising an amino acid sequence of Fig.  
1 or Fig. 2 comprising expressing the heterologous DNA in the transformed cellular hosts of a  
composition of claim 10 or 11.

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cont  
32. The method of producing a polypeptide according to claim 31 wherein said  
amino acid sequence is IGF-I and said nucleic acid sequence is sequence (a).

33. A method of producing a polypeptide according to claim 31 wherein said amino  
acid sequence is IGF-II and said nucleic acid sequence is sequence (b).

34. A method of producing a polypeptide according to claim 31, wherein said amino  
acid sequence is the amino acid sequence of Fig. 1 and said composition comprises the nucleic acid



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sequence:

5'-CTG GCG CTG TGC CTG CTC ACC TTC ACC AGC TCT GCC ACG GCT GGA CCG GAG  
ACG CTC TGC GGG GCT GAG CTG GTG GAT GCT CTT CAG TTC GTG TGT GGA GAC  
AGG GGC TTT TAT TTC AAC AAG CCC ACA GGG TAT GGC TCC AGC AGT CGG AGG  
GCG CCT CAG ACA GGT ATC GTG GAT GAG TGC TGC TTC CGG AGC TGT GAT CTA  
AGG AGG CTG GAG ATG TAT TGC GCA CCC CTC AAG CCT GCC AAG TCA GCT CGC  
TCT GTC CGT GCC CAG CGC CAC ACC GAC ATG CCC AAG ACC CAG AAG GAA GTA  
CAT TTG AAG AAC GCA AGT AGA GGG AGT GCA GGA AAC AAG AAC TAC AGG ATG-  
3'.

35. A method of producing a polypeptide according to claim 31, wherein said amino  
acid sequence is the amino acid sequence of Fig. 2 and said composition comprises the nucleic acid  
sequence:

5'-ATG GGA ATC CCA ATG GGG AAG TCG ATG CTG GTG CTT CTC ACC TTC TTG GCC  
TTC GCC TCG TGC TGC ATT GCT GCT TAC CGC CCC AGT GAG ACC CTG TGC GGC  
GGG GAG CTG GTG GAC ACC CTC CAG TTC GTC TGT GGG GAC CGC GGC TTC TAC  
TTC AGC AGG CCC GCA AGC CGT GTG AGC CGT CGC AGC CGT GGC ATC GTT GAG  
GAG TGC TGT TTC CGC AGC TGT GAC CTG GCC CTC CTG GAG ACG TAC TGT GCT  
ACC CCC GCC AAG TCC GAG AGG GAC GTG TCG ACC CCT CCG ACC GTG CTT CCG  
GAC AAC TTC CCC AGA TAC CCC GTG GGC AAG TTC TTC CAA TAT GAC ACC TGG  
AAG CAG TCC ACC CAG CGC CTG CGC AGG GGC CTG CCT GCC CTC CTG CGT GCC

*Sub E2*  
*D5*  
*cont*

CGC CGG GGT CAC GTG CTC GCC AAG GAG CTC GAG GCG TTC AGG GAG GCC AAA  
CGT CAC CGT CCC CTG ATT GCT CTA CCC ACC CAA GAC CCC GCC CAC GGG GGC  
GCC CCC CCA GAG ATG GCC AGC AAT CGG AAG TGA-3'

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36. The method of claim 31 wherein said heterologous DNA molecule is located on a plasmid that replicates in said host cells.

37. The method of claim 31 wherein said transformed cellular hosts are yeast.

38. The method of claim 31 wherein said transformed cellular hosts are *E. coli*.

39. The method of claim 31 wherein said transformed cellular hosts are *B. subtilis*.

40. The method of claim 31 wherein said transformed cellular hosts are *E. coli* strain HB101(phigf1).

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41. The method of claim 31 wherein said transformed cellular hosts are *E. coli* strain HB101(phigf2).

*D8*

42. A method according to claim 23 wherein the polypeptide is IGF-I and the polynucleotide sequence is sequence (a).

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43. A method according to claim 23 wherein the polypeptide is IGF-II and the polynucleotide sequence is sequence (b).

44. A vector comprising a nucleic acid sequence selected from the group consisting of the nucleic acid sequences (a), (b), (c), (d), and (e) of claim 1.

45. A vector according to claim 44 wherein said nucleic acid sequence is nucleic acid sequence (a).

46. An expression vector comprising a polynucleotide encoding a polypeptide, wherein said polypeptide comprises an amino acid sequence of Fig. 1 or Fig. 2, or fragments thereof, wherein said polynucleotide comprises a nucleic acid sequence encoding said amino acid sequence selected from the group consisting of the nucleic acid sequences (a), (b) and (d).

*D8 Cont*  
47. An expression vector according to claim 46, wherein said amino acid sequence is IGF-I.

48. An expression vector according to claim 46, wherein said amino acid sequence is IGF-II.

[ Please add the following new claim: ]